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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/551,764	10/03/2005	Young Min Kim	Q90374	4254
<div>23373 7590 05/22/2007</div> <div>SUGHRUE MION, PLLC</div> <div>2100 PENNSYLVANIA AVENUE, N.W.</div> <div>SUITE 800</div> <div>WASHINGTON, DC 20037</div>				
			<div>EXAMINER</div> <div>NIEBAUER, RONALD T</div>	
			<div>ART UNIT</div> <div>1609</div>	<div>PAPER NUMBER</div>
			<div>MAIL DATE</div> <div>05/22/2007</div>	<div>DELIVERY MODE</div> <div>PAPER</div>

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/551,764	KIM ET AL.	
	Examiner	Art Unit	
	Ronald T. Niebauer	1609	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 14 March 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-12 is/are pending in the application.
- 4a) Of the above claim(s) 12 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-11 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 03 October 2005 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>10/3/05 1/26/06</u> | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group I (claims 1-11) in the reply filed on 3/14/07 is acknowledged.

Claim 12 is withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 3/14/07.

During examination it was found that the search of the species of the invention as claimed was not burdensome so the election of species requirement has been withdrawn.

Drawings

The drawings are objected to because the content of figure 1 can not be determined. Lanes 1-3 of the gel are not clear and no features can be seen in these lanes. Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate

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changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

In addition to Replacement Sheets containing the corrected drawing figure(s), applicant is required to submit a marked-up copy of each Replacement Sheet including annotations indicating the changes made to the previous version. The marked-up copy must be clearly labeled as "Annotated Sheets" and must be presented in the amendment or remarks section that explains the change(s) to the drawings. See 37 CFR 1.121(d)(1). Failure to timely submit the proposed drawing and marked-up copy will result in the abandonment of the application.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-11 recite a PEG linker and a modification with one molecule of PEG. As claimed it is not clear if the PEG linker itself is a 'modification with one molecule of PEG', or if the modification is with a separate molecule of PEG. The overall ratio of PEG:protein is unclear since as claimed it could be, for example, 1:2 or 3:2. If the ratio is 3:2 how is the PEG addition controlled so that only one molecule attaches? Is the PEG linker a single PEG molecule or can there be multiple PEG molecules linking the protein molecules?

It is unclear based on claim 1 what the abbreviation PEG stands for. It would be remedial to amend the claim to include the phrase 'polyethylene glycol (PEG)'.

Claim 1 recites a physiological active polypeptide. How is the physiological activity determined? It is unclear if the term physiologically active refers to the PEG-polypeptide complex or to the polypeptide prior to addition of the PEG. The claim recites that the polypeptide is modified, does this modification alter the activity?

The term 'amino terminal' is unclear as used in claim 2. Does this refer to a single N-terminal residue or is it a broad term referring to a region or domain?

Claim 5 recites 'two ... groups at both ends'. Does this mean that there is a single group at each end (a total of two)? Does this mean that there are two consecutive groups at each of the ends?

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

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A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1,3,4,6,7,10, and 11 are rejected under 35 U.S.C. 102(b) as being anticipated by Braxton (US 5766897 as cited in the restriction requirement).

The current invention reads on a PEG-polypeptide homodimer complex as recited in claim 1 and related dependent claims limiting the polypeptide (claim 4), PEG linker molecular weight (claims 6-7), and the modifying PEG molecular weight (claims 10-11).

Braxton teaches a PEG-polypeptide dimeric complex (column 13 line 56) of the general formula R1-S-PEG-S-R2 where R1 and R2 may represent the same or different proteins. Braxton teaches claim 1 of the current application because the two protein molecules are connected via the PEG linker and the polypeptide is inherently modified by the same PEG molecule. Braxton also teaches that the complex is physiologically active as the complex retains 'substantially the same level of biological activity as that of the naturally-occurring, unmodified protein' (abstract). Braxton further teaches that PEG can be attached at particular residues (column 12 line 49) and mention that one PEG can be added to one protein (column 13 line 5). Braxton teaches that human growth hormone (Table IA and column 12 line 1) is a polypeptide that can be a part of the complex. Braxton further teaches that a lysine residue is typically reacted with PEG (column 2 line 12). Braxton teaches that the PEG linker/moiety may be in the range of 0.2-20 kDa (column 12 line 50). Therefore claims 1,3,4,6,7,10, and 11 are anticipated by Braxton.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 2,5,8, and 9 rejected under 35 U.S.C. 103(a) as being unpatentable over Braxton as applied to claims 1,3,4,6,7,10, and 11 above, and further in view of Kay et al. (US 2002/0077294).

As discussed above the current invention reads on a PEG-polypeptide homodimer complex as recited in claim 1 and related dependent claims limiting the PEG linker location (claim 2), PEG modifier location (claim 3), PEG linker groups (claim 5), PEG modifier groups (claim 8), and PEG modifier structure (claim 9).

Braxton teaches a PEG-polypeptide dimeric complex (column 13 line 56) of the general formula R1-S-PEG-S-R2 where R1 and R2 may represent the same or different proteins. Braxton teaches claim 1 of the current application because the two protein molecules are connected via the PEG linker and the polypeptide is inherently modified by the same PEG molecule. Braxton also teaches that the complex is physiologically active as the complex retains 'substantially the same level of biological activity as that of the naturally-occurring, unmodified protein' (abstract).

Braxton does not expressly teach specific PEG groups as recited in claims 2,5,8, and 9.

Kay et al. teach polypeptide derivatives in which a protein is linked to a nonproteinaceous moiety (e.g. a polymer) in order to modify properties (section 0146). Kay et al. teach PEG as an example of the polymer (section 0148). Kay et al. teach PEG modification at the amino terminus of the protein (section 0157). Kay et al. teach the polymer having a molecular weight of 2-100kDa (section 0149). Specifically, Kay et al. teach protein dimers via crosslinkers (section 0161). Kay et al. teach propionaldehyde (i.e. propionic aldehyde) groups on PEG (section 0148). Kay et al. teach reactive groups such as maleimide (section 0154). Kay et al. teach that the polymers may be branched or unbranched (section 0149).

Kay et al. teaches compositions of protein inhibitors and does not expressly teach the specific polypeptides of claim 4.

These references cover all elements of claims 2,5,8, and 9. Braxton teach nearly all elements of the claimed invention except details about the specific PEG groups. Kay et al. provide the remaining information.

Using PEG to modify proteins is well known in the art and one would be motivated to combine the work of Braxton with the work of Kay et al. due to the common subject area. It is noted in Braxton that the development of protein therapies is hampered by the short half-life of proteins after administration (column 1 line 46) and the use of PEG offers promise to help solve problems associated with protein therapies (column 1 line 60). Kay et al. also notes that chemically modified derivatives of a molecule may provide advantages such as increased stability (section 0156) and notes PEG as a chemical moiety for derivitization (section 0156).

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Further, one would have an expectation for success since Kay et al. simply expand upon the work of Braxton et al. Taken together, it would have been obvious to one of skill in the art to make the invention of the current application.

A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. (*In re Opprecht* 12 USPQ 2d 1235, 1236 (Fed Cir. 1989); *In re Bode* 193 USPQ 12 (CCPA) 1976). In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a). From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Double Patenting

Application 10807732 is noted of interest. As currently amended (3/21/07) a double patenting rejection is not appropriate, although a provisional nonstatutory obviousness-type double patenting rejection would have been appropriate for Application 10807732 as originally claimed.

Conclusion

Patent 6106828 as disclosed in the IDS is noted of interest.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ronald T. Niebauer whose telephone number is 571-270-3059. The examiner can normally be reached on Monday-Thursday, 7:30am-5:00pm, alt. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mary Mosher can be reached on 571-272-0906. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

rtn



MARY MOSHER
SUPERVISORY PATENT EXAMINER

5-21-07